Von Willibrand Factor in Cirrhotic Patients Undergoing Oesophageal Varices Band Ligation

Thesis

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بسم الله الرحمن الرحيم

قالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا

عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
AASLD	Association of Study for the Liver Diseases
AKI	Acute Kidney Injury
ALT	Alanine amino-transferase
Anti-HBc	Antibodies against HBV's core antigen
Anti-HBs	Antibodies against HBV's surface antigen
Anti-HCV	Antibodies against HCV
AST	Aspartate transaminase
BCLC	The Barcelona-Clínic Liver Cancer
CTP	Child-Turcotte-Pugh score
DHS	Demographic and Health Survey
DVR	Delayed virological response
EASL	European Association for the Study of the Liver
EMA	European Medicines Agency
EVR	Early virological response
FDA	Food and Drug Administration U.S.
HBs Ag	HBV surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HCW	Health Care Workers
IDUs	Intravenous Drug Users
IEC	Information-Education-Communication
MELD	Model for End-stage Liver Disease
MOHP	Ministry of Health and Population Egy.
NBTC	National Blood Transfusion Center Egy.

List of Abbreviations (Cont...)

Abb.	Full term
NIH	National Institutes of Health U.S.
OV	oesophageal varices
PAT	Parenteral Antischistomal Therapy
PCR	Polymerase Chain Reaction
PegINF	Pegylated Interferon
PEP	Post-exposure prophylaxis
Plt	Platelets
RBV	Ribavirin
RCTs	high-quality Randomized Controlled Trials
RVR	Rapid virologic response
SVR	Sustained Virologic Reponse
TACE	Transarterial Chemoembolisation
TNM	Tumor Node Metastasis
vWD	Von Willebrand disease
WHO	World Health Organization

Introduction

Portal hypertension is a serious consequence of cirrhosis that may result in life-threatening complications with increased morbidity and mortality ***(Bosch and Garcia-Pagan, 2000).***

In cirrhotic livers, increased resistance to portal blood flow is the primary factor in the pathophysiology of portal hypertension(PHT) and is caused by structural abnormalities in the hepatic vascular architecture and an increased hepatic vascular tone ***(Gracia-Sancho et al., 2008).***

The endothelium plays a pivotal role modulating vascular tone and inflammatory processes via the release of nitric oxide, which has vasodilatory, anti-inflammatory and antithrombotic properties. Endothelial dysfunction is an early key event in many vascular diseases and is considered a major determinant of the increased hepatic vascular tone of cirrhotic livers ***(Iwakiri and Groszmann, 2007).***

The current gold standard for measuring PHT and its severity is measurement of the hepatic venous pressure gradient (HVPG) ***(Groszmann et al., 2005).*** HVPG is also emerging as a reliable endpoint to assess disease progression and therapeutic response in chronic liver disease. HVPG measurement is safe and relatively simple to perform, it is invasive, costly, and only performed in specialist centres ***(Thalheimer et al., 2011).*** A recommendation from the Baverno V Consensus Workshop

on Methodology of Diagnosis and Therapy in PHT was to identify noninvasive tools for detecting PHT ***(De Franchis, 2010)*** which could have clinical utility for monitoring changes in PHT over time.

Von Willibrand Factor (vWF) is a large adhesive protein released by activated endothelial cells and therefore represents an indicator of endothelial cell activation ***(Van Mourik et al., 1999)*** which is easy to measure ***(Deanfield et al., 2007).*** Levels of vWF are increased in patients with cirrhosis and correlate with the severity of liver disease ***(Lisman et al., 2002).***

Aim of the Work

The main aim is to study the effect of band ligation on vWF level as a marker of portal hypertension in patients with liver cirrhosis.

Chapter one

Cirrhosis

Introduction and definition:

The liver is the largest internal organ of the body, with blood supply from both hepatic artery and portal vein. The liver performs many functions including synthesis of most serum proteins, regulation of glucose and lipids, and production of bile ***(Am, 2009).***

These essential functions become impaired when a liver develops cirrhosis, Cirrhosis represents the end stage of any chronic liver disease. Hepatitis C and alcohol are currently the main causes of cirrhosis in the United States ***(Am, 2009).***

Cirrhosis is defined pathologically by the loss of normal microscopic lobular architecture with fibrosis and nodular regeneration. Chronic liver disease –including hepatitis C and cirrhosis- is currently a leading cause of death and the most common cause of portal hypertension ***(Dego, 1999).***

Pathogenesis of Cirrhosis:

Liver fibrosis or cirrhosis is a common progressively pathological lesion of chronic liver diseases in response to various liver-damaging factors. The main mechanisms of fibrotic or cirrhotic initiation and progression at the level of cellular and molecular events have been elucidated in the past two decades ***(Friedman 1993).***

Various causes, including hepatitis virus infections, toxification, ischemia, congestion, parasites infection, abnormal cooper or iron load, etc, result in chronic inflammation and/or wound healing responses, of which the main characteristics manifest is the absolute increase of the excessive extracellular martrix (ECM) synthesis and the relative decrease of them, leading to ECM deposit ***(Liu et al., 1997).***

With the stimulation of inflammation or toxins, activated hepatic stellate cells (Ito cells), injuried or regenerated hepatocytes, Kupffer cells, sinusoidal cells and natural killer (NK) cells produce certain cytokines or immunoreactive factors, which exert various biological effects on their respective target cells or organs in an autocrine or paracrine manner ***(Bissell, 1998).***

These consist of the cellular basis of hepatic fibrosis advances. The unblocked progressively pathological lesions with inevitably result in, lobular reconstruction, pseudolobule formation and nodular regeneration ***(Bissell, 1998).***

Causes of Cirrhosis:

Cirrhosis represents the end stage of any chronic liver disease caused by various causes, including virus infections, toxification, ischemia, congestion, parasites infection, abnormal cooper or iron load, autoimmune disease and others ***(Friedman, 1993).***

Common causes of chronic liver disease in the United States are:

- Hepatitis B or C infection
- Alcohol abuse

Less common causes of cirrhosis include:

- Autoimmune hepatitis
- Bile duct disorders
- Some medicines
- Hereditary diseases
- Other liver diseases such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

(Mehta et al., 2009)

Clinical presentation and diagnosis:

Cirrhosis is often an indolent disease, and the condition often is discovered during a routine examination with laboratory or radiographic studies, or at autopsy ***(Friedman et al., 2004).***

Many patients remain asymptomatic until the occurrence of decompensation, characterized by ascites, variceal bleeding, spontaneous bacterial peritonitis (SBP), or hepatic encephalopathy (HE) ***(Friedman et al., 2004).***

In a patient with any chronic liver disease, finding a palpable left lobe of the liver (hard and nodular) and a small